

Aminoacid-linked C₆₀ Fullerene Derivatives as Novel Inhibitors of Nitric Oxide Synthase

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Nitric oxide synthase, NOS is a complex flavin and heme-containing oxido-reductase specialized in oxidizing L-Arginine to produce nitric oxide, a versatile signaling cellular molecule. In recent papers, the inhibition of NOS by various water-soluble fullerenes was reported^{1,2}. To gain further insight into this process, we synthesized novel C₆₀ fullerene mono-adducts carrying several aminoacid moieties, as close structural analogs of the natural substrate of the enzyme (L-Arginine). These derivatives offer the possibility to investigate whether the aminoacid attached to the C₆₀ cage interacts with the active site of the enzyme. At the same time, the free zwitterionic group of α -aminoacids employed confers a degree of water-solubility.

The synthetic routes we employed, the azide cycloaddition and Bingel cyclopropanation generated three types of derivatives: triazolines, related aza-fulleroids, and malonates. Hence, the aminoacid residue was anchored to the C₆₀ core by 6,6-triazolino-, 5,6-aza- or 6,6-methano- structures. These anchors confer to C₆₀ derivatives different electroreductive potentials. If the reduction of fullerenes is involved as an underlying mechanism in the inhibition of NOS, by interfering with its native electron transfer, derivatives with stronger electron acceptor properties would behave as more potent inhibitors. The impact of this factor was investigated by kinetic enzymatic studies on nitric oxide synthase.

References:

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